REMARKS

Claims 34-37, 39, 41, 43, 44, and 71-73, as amended, remain herein.

1. Claims 34-37, 39, 41, 43, 44 and 72 were rejected under 35 USC §112, paragraph 1, as allegedly failing to comply with the written description requirement, the Office Action alleging that the phrase "freestanding retention therein indefinitely" in claim 34 was new matter not described in the specification.

It is true that the specific words "freestanding retention therein indefinitely" do not appear in haec verba in applicants' specification. However, one skilled in the relevant art would understand that the written description in applicants' specification conveys the substance of that phrase. This is demonstrated by the disclosures of the prior references cited in the same Office Action. Coniglione U.S. Patent 5,713,828 (which is expressly cited at page 3, line 5 of applicants' specification) explains "Brachytherapy that uses long-term or permanent implantation, [wherein] the radioactive device is usually referred to as a 'seed.'" ('828, col. 2, lines 18-20). The '828 specification goes on to state that "where the radiation seed is implanted directly into the diseased tissue, the form of therapy is referred to as interstitial brachytherapy." ('828, col. 2, lines 20-22). Still further, '828 discusses the fact that "permanently implanted brachytherapy devices . . . [have] no means of affirmatively localizing the device. . . ." ('828, col. 2, lines 29-31; emphasis added here). And, see generally, Coniglione '828, col. 2, line 18 through col. 3, line 60, describing various forms of interstitial brachytherapy.

Likewise, Sioshansi U.S. Patent 6,030,333 describes discreet seeds individually implanted at a treatment site. ('333, col. 1, lines 61-63). And, see generally Sioshansi '333, col. 1, line 50 through col. 2, line 45.

Thus "permanent" implantation of discreet, individual seeds, freestanding within the surrounding tissue for indefinite periods of time, is indeed what those skilled in the relevant art understand interstitial delivery of seeds to mean.

And, applicants' written description expressly indicates that it is related to the interstitial delivery of small hollow seeds. See, for example, applicants' disclosure at page 7, lines 2-10:

> According to the present invention, the small hollow seed, e.g., made of metal, is delivered to a precise site in a tissue, e.g., a tumor, by interstitial delivery methods such as implantation gun, syringe, or catheter, which methods further include visual confirmation, e.g., by stereotaxy, ultrasound, CT or MRI guidance, to ensure precise (millimeter precision) placement of seeds. These seeds, preferably made of metal or polymeric material, will be of a hollow configuration having one or more holes disposed therein that enable the hollow seed to be effectively delivered to desired sites, wherein they release a therapeutic agent (e.g., nucleic acid sequence) by diffusion. [emphasis added here]

Thus, regardless of the particular words used, it is clear that applicants' claimed delivery device consists of a hollow seed for interstitial implantation into a tissue or organ for freestanding retention therein indefinitely. If the PTO so desires, applicant can add those specific words to applicants' disclosure, leaving those words in claim 34, or applicant can remove those specific words from claim 34 – either alternative not changing the scope of either applicants' written description or claims. As demonstrated above herein, the words "freestanding retention therein indefinitely" would be understood by those skilled in this art to be supported by applicants' written description. Accordingly reconsideration and withdrawal of this rejection are respectfully requested.

2. Claims 34-37, 39, 41, 43, 44 and 71-73 were rejected under 35 USC §112, paragraph two, as allegedly indefinite in the use of the term "substantially" hollow in claims 34 and 71, and

the words "to provide for" therein. Both of claims 34 and 71 have been amended to delete the word "substantially", to delete the words "to provide," and to rearrange the language of the claim so that the "therapeutic agent" is expressly claimed as an element of the claimed drug delivery device. These amendments moot the grounds of rejection stated in the Office Action. Accordingly reconsideration and withdrawal of this rejection are respectfully requested.

3. Claims 34, 36 and 71 were rejected under 35 USC §102(b) over the Merriam-Webster (Third New) International Dictionary (1963). While the Office Action does not more specifically identify the portion of the dictionary allegedly relied upon, it does mention "definition 4b" and an underscored portion of definition 4b of the word "seed" was provided with the Office Action. That definition 4b is quoted, in its entirety, below:

> 4: . . .b: a small usu. glass and gold or platinum capsule used as a container for a radioactive substance (as radium or radon) to be applied usu. interstitially in the treatment of cancer

The rejection alleged under §102 in the Office Action is woefully lacking in basis. The cited dictionary definition does not even mention "a drug delivery device" as recited in the preamble words of applicants' independent claims 34 and 71. Nor does the dictionary definition in any way describe a hollow seed "having an opening at each thereof, said openings being sized and arranged . . . for the controlled diffusion of a therapeutic agent . . . ." Still further, the dictionary definition nowhere even remotely suggests that the seed described in the dictionary definition includes a "therapeutic agent comprising a radionuclide and (1) a nucleic acid sequence, or (2) a protein or polypeptide" as expressly recited in applicants' claim 34, or a "therapeutic agent comprising a radionuclide and (1) a viral vector comprising a nucleic acid sequence, or (2) a protein or polypeptide," as expressly recited in applicants' claim 71. The

dictionary definition cited in the Office Action does not even come close to disclosing all elements of applicants' claims. Accordingly reconsideration and withdrawal of this rejection are respectfully requested.

4. Claims 34-37, 39, 41, 43, 44 and 71-73 were rejected under 35 USC §103(a) as allegedly obvious over Rashid British Patent 2,243,777 [GB '777] in view of Sioshansi U.S. Patent 6,030,333.

Rashid GB '777 discloses a device for sustained release of an active ingredient when the device is in contact with body fluids, which device includes a chamber containing the active ingredient and having an outlet therefrom; a capillary bore extending from the outlet for controlling the rate of release of the active ingredient from the chamber into body fluid, wherein the length and diameter of the bore are the controlling factors determining the release rate of the active ingredient into the body fluid. Rashid emphasizes the importance of the capillary bore stating that "the rate of release of active ingredient from the device is then controlled predominantly by the length and diameter of the capillary bore, rather than by the rate of dissolution of the active ingredient or any other factor." (GB '777, page 2, lines 18-21). The Rashid device may have one or more outlets each provided with its own capillary bore. (GB '777, page 4, lines 17-19). If required, the open end of the capillary bore may be provided with a "copy" of sugar or gelatin which dissolves away on administration, or the bore may be filled with a soluble material which dissolves away on administration, thereby facilitating ingress of body fluids into the capillary tubing. Rashid discloses that the active ingredient within the device may be a medicament, contraceptive, or for prophylactic, diagnostic or nutritional use. (GB '777, page 5, last two lines).

The Office Action, page 7, first paragraph, expressly admits that Rashid does not disclose that the active ingredients are "a radionuclide and a nucleic acid sequence, protein or polypeptide."

The Office Action fails to acknowledge that applicants' independent claims 34 and 71 recite a drug delivery device consisting of only the recited elements which follow. As a matter of law, appellants' claims are limited to those recited elements, which do not include any capillary bore which is required by, and perhaps the most critical element of, the Rashid GB '777 device.

Sioshansi '333 discloses an implantable radiotherapy device. A traditional form of such device is illustrated in Sioshansi's Fig. 1 wherein a lead x-ray marker and Pd-103 plated graphite pellets are sealed within a titanium tube. Sioshansi '333 discloses a number of other devices which allegedly obviate the disadvantages of prior art radiotherapy seeds and encapsulated films, which employ a biocompatible radiotherapy delivery vehicle or template and at least one source of radiation incorporated directly into a portion of the template to render that portion radioactive. A variety of shapes of such templates are disclosed. Such devices may be permanently or temporarily implanted.

Contrary to the impression given in the Office Action, page 7, second paragraph, Sioshansi is not directed to implantable seeds, but to a template device for rendering seeds obsolete. The Office Action also points to Sioshansi's ability to deliver both radiation and non-radiation treatments together by applying on the surface of one or more portions of his templates therapeutic agents including biological agents such as proteins and growth factors. Such agents can be applied either directly onto the radioactive template, or onto the encapsulated coating 22 over the radioactive template, as desired for the specific application. ('333, col. 11, lines 53-63).

The Office Action relies upon '333, col. 12, lines 57-61, which refer to radioisotopes such as low-energy gamma ray emitters. "Candidates might include, for example, ^{45}Ca, ^{123}Sn, ^{89}Sr, ^{32}P, ^{33}P, ^{103}Pd, and ^{125}I, although there other possibilities." ('333, col. 12, lines 60-62).

However, the Office Action fails to acknowledge that Sioshansi is not directed to interstitially implantable seeds, and particularly not to hollow seeds. Rather, Sioshansi is directed to templates which incorporate a source of radiation directly into the material of the template, thus forming a substantially sealed radiation source without the need for encapsulation of either the radiation source or the device. See '333, col. 4, lines 13-19. Furthermore, the Sioshansi device, as explained immediately above, is definitely not "for the controlled diffusion of the therapeutic agent which agent comprises a radionuclide and (1) a nucleic acid sequence, or (2) a protein or polypeptide," (as recited in applicants' claim 34), or "a radionuclide and (1) a viral vector comprising a nucleic acid sequence, or (2) a protein or polypeptide" (as recited in applicants' claim 71). Applicants' claimed drug delivery device is expressly constructed for controlled diffusion of both a radionuclide and a nucleic acid sequence or vector comprising same, whereas the prior art uniformly encapsulates and seals radioactive sources in any such implantable devices.

Rashid discloses a device which becomes unsealed by dissolution of plugs which initially block the required capillary bores thereof, and Rashid does not disclose diffusion release of radioactive therapeutic agent materials. Sioshansi discloses the use of radioactive therapeutic materials which are incorporated into the template material of his device, thus forming a substantially sealed radiation source without the need for encapsulation of the radiation source or device. Applicants' claimed invention expressly provides controlled diffusion of the therapeutic agent which includes both a radionucleotide and a nucleic acid sequence, protein or polypeptide.

That is, contrary to the fundamental and uniform teaching of the prior art that the radioactive material in implantable devices should be sealed or encapsulated, in applicants' device the radionucleotide material is specifically intended to diffuse from the delivery device into the tissue or organ into which such device is implanted inter vivo.

Neither Rashid GB '777, nor Sioshansi '333 discloses all the elements of applicants' claimed invention. Furthermore, there is no disclosure or teaching in either Rashid or Sioshansi, or anything else in this record of anything that would have suggested combining portions of their disclosures effectively to anticipate or suggest applicants' claimed invention to one of ordinary skill in this art. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

5. Claims 34-37, 39, 41, 43-44 and 71-73 were rejected under 35 USC §103(a) as obvious over Coniglione '828 in view of Sioshansi '333.

Coniglione discloses a hollow tube brachytherapy device as illustrated in Figs. 1A, 1B, 2A and 2B wherein a metallic tube has a layer 104, 204 of radioactive material coated thereon, covered by an electroplated sealing layer 106, 206. Coniglione explains that the tubular devices have a hollowed lumen, and may have other openings therein, but "the entire device is provided with a biologically compatible, radiation-permeable, surface-sealing layer that entirely seals the external surface of the two." ('828, col. 4, lines 40-42; emphasis added here).

The Office Action acknowledges that Coniglione does not specify the incorporation of a nucleic acid, protein or polypeptide. The Office Action again fails to acknowledge that applicants' claim recites a drug delivery device consisting of only the recited elements. And, the Office Action fails to acknowledge that, as cited above, the Coniglione device is always sealed.

Quite differently, applicants' claimed device includes openings in the hollow seed which are specifically intended to permit controlled diffusion of the therapeutic agent out of the hollow seed, and that therapeutic agent includes a radioactive radionuclide, as well as a nucleic acid sequence, protein or polypeptide.

The earlier description and discussion of Sioshansi '333 above herein are equally applicable in traversing Sioshansi as an alleged basis for the present rejection.

Neither Coniglione nor Sioshansi discloses or suggests an interstitially implantable hollow seed having openings therein expressly for the controlled diffusion of a therapeutic agent which includes a radioactive radionuclide and a nucleic acid sequence, protein or polypeptide.

There is simply no disclosure or teaching in any of Coniglione or Sioshansi, or anything else in this record which discloses applicants' claimed invention. Nor is there any disclosure in any of those references which would have suggested to one of ordinary skill in the art modifying or combining any portions thereof effectively to anticipate or suggest applicants' presently claimed invention. Accordingly reconsideration and withdrawal of this rejection are respectfully requested.

For all the foregoing reasons, all claims 34-37, 39, 41, 43, 44 and 71-73 are now proper in form and patentably distinguished over all grounds of rejection cited in the Office Action. Accordingly, allowance of all claims is respectfully requested.

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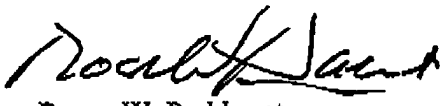
The PTO is hereby authorized to charge/credit any deficiency/overpayment to Deposit Account. No. 19-4293 (Order No. 28964.0054). Should the Examiner believe that further changes would place this application in even better condition for allowance, the Examiner is invited to telephone applicants' undersigned attorney.

Respectfully submitted,



Roger W. Parkhurst
Registration No. 25,177

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STEPTOE & JOHNSON LLP
1330 Connecticut Avenue, N.W.
Washington, DC 20036
Telephone: (202)429-3000
Facsimile: (202) 429-3902

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By: Hortense G. Coleman